close-down in clinical research," says Tim Dyer, chief executive of Addex Therapeutics, a biotechnology company based in Geneva, Switzerland. "The health-care systems will simply be overloaded." On 18 March, Addex announced that it would delay the start of a clinical trial to treat involuntary movements in people with Parkinson's disease.

At Yale University in New Haven, Connecticut, lung-cancer researcher Roy Herbst says clinical trials for cancer have been cut to "almost zero" and are allowed only when a participant is deemed to have exceptional need.

"The whole process has really ground to a halt," he says, "and I feel bad because there are patients who might have benefited from those trials."

But the measures are necessary, he adds. Many people with advanced cancer are vulnerable to infection, and trips to the clinic for treatment and assessments could be deadly if patients are exposed to the coronavirus.

Herbst has had to ask three-quarters of his colleagues in the oncology department at Yale to stay away from the hospital to minimize their risk of infection. Instead, they are being held in reserve to treat people with COVID-19 if the first round of clinicians become infected. Even routine procedures such as biopsies, sometimes required for enrolment in a clinical trial, are now difficult to schedule as hospitals struggle with personnel and equipment shortages.

Agencies adapt

Government agencies have released guidance for investigators who need to suspend or modify trials. The US Food and Drug Administration, for example, has issued guidance for trials that might have to pause, change their study plans or make do with incomplete data because of the COVID-19 pandemic. Ethics committees are working overtime as researchers file requests to alter their clinical-trial plans in ways that minimize how often participants need to venture into the clinic, says Barbara Bierer, who directs the Multi-Regional Clinical Trials Center of Brigham and Women's Hospital and Harvard in Boston, Massachusetts.

Agencies and funders have shown remarkable flexibility, says Charles Blanke, an oncologist at Oregon Health & Science University in Portland and leader of the publicly funded SWOG Cancer Research Network. The US National Cancer Institute announced on 23 March that it would allow the investigators it funds to assess trial participants' health remotely where possible. Some doctors' assessments may be carried out over video calls, and some audits of clinical-trial procedures will be conducted virtually, with inspectors examining the paperwork online rather than visiting the clinic to assess standards.

The rapid release of these guidelines is a particular relief because many clinical-trial sites did not plan for a pandemic such as that of COVID-19, says Blanke, despite warnings from experts that one was inevitable. After this outbreak, he says, clinical researchers will be better prepared, and the increased capacity for virtual visits will be a lasting boon to both researchers and patients.

For now, it's unclear what long-term effects the outbreak will have on drug regulation. "There will be a disruption, obviously," says Bierer. "And whether that delay manifests in delaying final approvals is unknowable today."

It's that uncertainty that haunts Nizar. She worries that her concerns might sound selfish in the face of the global suffering caused by the pandemic. But she also knows that the delay to her clinical trial could last well beyond the months of social isolation and lockdowns.

Her best hope now, she says, is that regulators will learn from the speed and urgency with which a candidate vaccine for the COVID-19 virus has been rushed into clinical trials, forgoing some of the usual pre-trial animal tests. Nizar wants to see therapies for rare diseases treated with the same urgency.

"Our lives have always been in panic mode," she says. "Now the world has a glimpse into what our reality is."

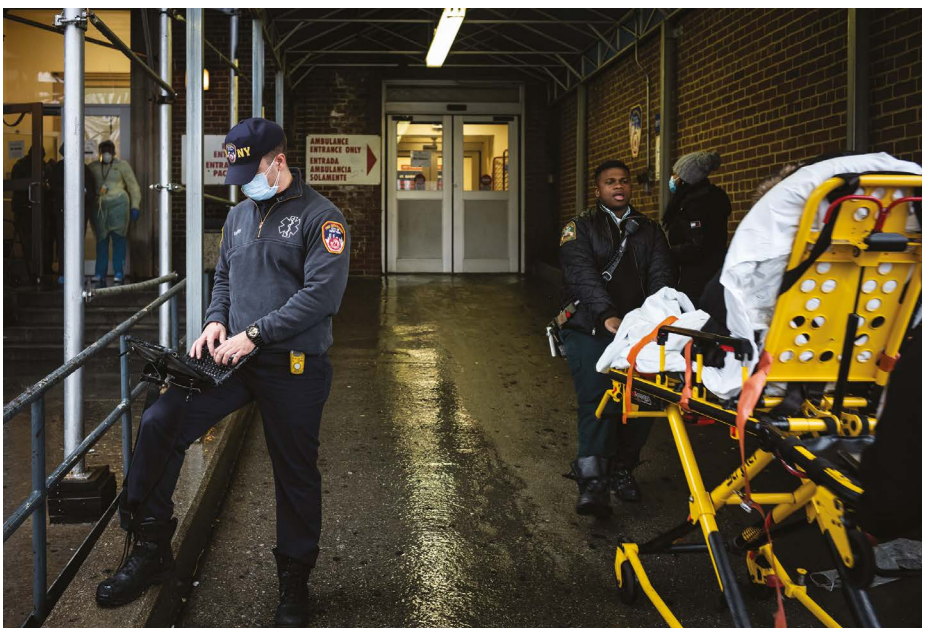
HOW BLOOD FROM COVID-19 SURVIVORS MIGHT SAVE LIVES

New York City researchers hope antibody-rich plasma can keep people out of intensive care.

By Amy Maxmen

Hospitals in New York City are gearing up to use the blood of people who have recovered from COVID-19 as a possible antidote for the disease. Researchers hope that the century-old approach of infusing patients with the antibody-laden blood of those who have survived an infection will help the city — now the US epicentre of the outbreak — to avoid the fate of Italy, where intensive-care units (ICUs) are so crowded that doctors have turned away people who need ventilators to breathe.

The efforts follow studies in China that infused patients with plasma — the fraction of blood that contains antibodies, but not red blood cells — taken from people who had recovered from COVID-19. But these studies have reported only preliminary results so far. The 'convalescent plasma' approach has also seen modest success during outbreaks



MISHA FRIEDMAN/GETTY

Hospitals in New York City are becoming overwhelmed with coronavirus cases.

of severe acute respiratory syndrome (SARS) and Ebola — but US researchers are hoping to increase the value of the treatment by selecting donor blood that is packed with antibodies and giving it to people most likely to benefit.

A key advantage of convalescent plasma is that it's available immediately, whereas drugs and vaccines take months or years to develop. Infusing blood in this way seems to be relatively safe, as long as it is screened for viruses and other infectious agents. Scientists who have led the charge to use plasma want to deploy it now as a stopgap measure, to keep serious infections at bay and hospitals afloat as a tsunami of cases comes crashing their way. "Every patient that we can keep out of the ICU is a huge logistical victory because there are traffic jams in hospitals," says Michael Joyner, an anaesthesiologist and physiologist at Mayo Clinic in Rochester, Minnesota.

Thanks to the researchers' efforts, the US Food and Drug Administration announced last week that it will permit the emergency use of plasma for patients in need. As early as this week, at least two hospitals in New York City — Mount Sinai and Albert Einstein College of Medicine — hope to start using survivor plasma to treat people with the disease, Joyner says.

After this first roll-out, researchers hope the use will be extended to people at a high risk of developing COVID-19, such as nurses and physicians. For them, it could prevent illness so that they can remain in the hospital workforce, which can't afford to be depleted.

Hard evidence

At the same time, US academic hospitals are planning to launch placebo-controlled clinical trials to collect hard evidence on how well the treatment works.

Liise-anne Pirofski, an infectious-disease specialist at Albert Einstein College of Medicine, says that, in one proposed trial, researchers plan to infuse patients at an early stage of the disease and see how often they advance to critical care. Another trial would enrol people with severe infections. A third would explore plasma's use as a preventive measure for people in close contact with those confirmed to have COVID-19, and would evaluate how often such people fall ill after an infusion, compared with others who were similarly exposed but not treated. These outcomes can be measured within a month, she says. "Efficacy data could be obtained very, very quickly."

Even if it works well enough, convalescent serum might be replaced by modern therapies later this year. Research groups and biotechnology companies are identifying antibodies against the coronavirus, with plans to develop these into precise formulas. "The biotech cavalry will come on board with isolating antibodies, testing them, and developing drugs and vaccines, but that takes time," says Joyner.

Q&A

Should we infect healthy people with coronavirus?

With no end to the coronavirus pandemic in sight, researchers are discussing a dramatic approach that could help to end it: infecting a handful of healthy volunteers with the virus to speed up vaccine testing.

Many scientists see a vaccine as the only solution to the pandemic. At least one candidate is in safety trials, but a major hurdle is showing that a vaccine works. This typically requires large studies in which thousands of people receive a vaccine or a placebo, and researchers track who becomes infected naturally.

It would be quicker to do a 'human challenge' study, argue scientists in a March preprint (N. Eyal *et al*. Preprint at DASH http://go.nature.com/33y1hey; 2020). This would involve exposing healthy people to the virus and seeing whether those who are vaccinated escape infection.

Nir Eyal, the director of the Center for Population-Level Bioethics at Rutgers University in New Brunswick, New Jersey, and co-author of the preprint, tells *Nature* how the study could be done.

Why should we consider human-challenge studies of coronavirus vaccines?
They could greatly accelerate the time to approval and potential use. Testing vaccines in phase III trials takes a long time. That's done on many people, some of whom get the vaccine and some of whom get placebos or competing vaccine candidates. Researchers then look for differences between these groups in infection rates.

> **"There are some historical precedents for exposure to very deadly viruses."**

But many people will try to be careful in this outbreak — by self-isolating, say — and it will take a very long time until interpretable results emerge. If, instead, one exposes all study participants to the pathogen, one can not only rely on far fewer volunteers but, more importantly, take a much shorter period to get results.

Are there any precedents for infecting healthy people with a pathogen?
We do human-challenge studies for less deadly diseases quite frequently — for example, for influenza, typhoid, cholera and malaria. There are some historical precedents for exposure to very deadly viruses. The thing that demarcates the design that we propose from some of these historical instances is that we feel there is a way to make these trials surprisingly safe.

How could you conduct such a study?
You would start only after some preliminary testing to ensure that a vaccine candidate is safe and that it raises an immune response in humans. You then gather a group of people at low risk from any exposure — young and healthy individuals — and ensure that they are not already infected. You give them either the vaccine candidate or a placebo and wait for an immune response. Then you expose them to the virus.

You follow all the participants closely to catch any signs of infection as early as possible. You are trying to check whether the vaccine group is doing better than the placebo group. That might be in terms of viral levels, the time until symptoms emerge or whether they're infected or not.

Is this ethical?
It might seem that anybody volunteering to participate in such a study lacks capacity for rational decision-making. But humans do many important things out of altruism. And although the study introduces risks, it also removes them. And the net risks, although unclear, are not clearly extremely high. So, it is potentially rational — even from a selfish point of view — to participate in such a study.

We also let humans volunteer to do risky things all the time; for example, to be in the emergency medical services during this period. That elevates their risk of getting infected but it's very important. In this case, vaccines could be our societies' only way out of the bind between economic stagnation and widespread mortality.

Interview by Ewen Callaway
This interview has been edited for length and clarity.